HEPATOBILIARY ABNORMALITIES IN AIDS PATIENTS

DISSERTATION SUBMITTED FOR
THE FULFILLMENT OF
DOCTOR OF MEDICINE
BRANCH I – GENERAL MEDICINE

MARCH 2007

THE TAMILNADU DR.M.G.R. MEDICAL UNIVERSITY
CHENNAI, TAMILNADU.

CERTIFICATE

This is to certify that this dissertation entitled **"HEPATOBILIARY ABNORMALITIES IN AIDS PATIENTS"** submitted by **Dr. C. ANANDI** to The Tamil Nadu Dr.M.G.R. Medical University, Chennai is in partial fulfillment of the requirement for the award of M.D. degree Branch I (General Medicine) and is a bonafide research work carried out by her under direct supervision and guidance.

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DECLARATION

I, **Dr. C. ANANDI** declare that I carried out this work on **"HEPATOBILIARY ABNORMALITIES IN AIDS PATIENTS"** at Department of General Medicine, Government Rajaji Hospital during the period of January 2005 – September 2006. I also declare this bonafide work or a part of this work was not submitted by me or any other for any award, degree, diploma to any university, board either in India or abroad.

This is submitted to the Tamilnadu Dr.M.G.R. Medical University, Chennai in partial fulfillment of the rules and regulation for the M.D. in General Medicine Degree examination.

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ACKNOWLEDGEMENT

At the outset, I thank our Dean **Prof. Dr. S.M. Sivakumar M.S.,** for permitting me to carry out this study in our hospital.

I am greatly indebted to my beloved Chief & Head of the Department **Prof. Dr. Nalini Ganesh, M.D.,** for her guidance, encouragement and support during the study period.

I am obliged to **Prof. Dr. R.Ganesh, M.D. (D.V)** Head of the Department of STD for his valuable suggestion and guidance

I sincerely thank **Prof.Dr.L.Thayumanavan**, Head of the Department, Medical Gastro enterology, for motivating me in taking up this research.

I acknowledge the support extended by **Dr.M.R.Parthasarathy,** Medical Officer, ART Centre, GRH, Madurai.

I express my gratitude to Assistant Professors **Dr.V.T.Premkumar,M.D, Dr.M. Sooriyakumar, M.D, and Dr.V.Ganesh Pandian, M.D. Dr. Sivakumar, M.D.** for their valuable suggestion

Above all I gratefully acknowledge to all the patients who participated in the study for their co-operation without which this work would not have been possible.

CONTENTS

INTRODUCTION

Acquired Immuno Deficiency Syndrome (AIDS) was first recognized in 1981, manifested by the opportunistic infections and malignancy (pneumocystis carinii pneumonia, kaposi's sarcoma) in homosexual men. In 1983, French scientist Prof. Luc Montagnier and his co –workers isolated the causative viral agent, which was later named as Human Immunodeficiency Virus.[1] In 1985, a sensitive enzymes linked immunosorbant assay (ELISA) was developed.

In 1986, Montagnier's group discovered a new type of HIV in West Africa and labeled it as HIV-2.[2] The origin of the virus is unclear. The most likely scenario is that the HIV was introduced into human from another primate in Sub –Saharan Africa.[3]

WHO and UNAIDS estimate that at the end of 2001, 40 million people around the world were living with HIV.[4] India is now considered the country with the largest number of infected persons in the world.[5] India alone accounts for 4 million cases. The spread mainly occurs through heterosexual route.

The HIV epidemic is generalized in 6 Indian states-Maharashtra, Tamil Nadu, Karnataka, Andhra Pradesh, Manipur and Nagaland. In Tamil Nadu, almost 5 lakh people are infected with HIV and the infection rate is 3 times higher in the villages than in the cities.

ETIOLOGY:

Human Immuno Deficiency Virus (HIV) is a lymphotrophic human retro virus. It is a RNA virus with icosahedral structure. The hallmark of the virus is the reverse transcription of the genome RNA to DNA inside the host cell by the enzyme reverse transcriptase.

INCUBATION PERIOD:

Incubation period of Acute Primary HIV infection (Acute Sero-conversion Syndrome) is within 3-4 weeks. Average period to develop AIDS is 8-10 years. The documented cytopathic effect is 50- 80 cells/microlitre per years.

PROBABILITY OF HIV-1 INFECTION PER EXPOSURE

MODE OF INFECTION	INFECTION PER EXPOSUR
Male to female ,unprotected vaginal sex	0.1% to 0.2%
Female to Male, unprotected vaginal sex	0.03% to 0.1%
Male to Male, unprotected anal sex	0.5 to 3%
Needle stick	0.3%
Mother to child transmission	13 to 48%
Exposure to contaminated blood products	90 to 100 %

MOLECULAR EPIDEMIOLOGY OF HIV:

The diversity of the global AIDS pandemic is also reflected in the heterogenecity of the viral subtypes or clades of HIV. According to

DNA sequence data, HIV-1 can be divided into three major groups. Group M (major) which contains ten genetically distinct subtypes- A to J Group O (outlier) which contains several heterogeneous virus. Group N (Cameroontype).

In addition there are at least 5 subtypes of HIV –2, the predominant virus in West Africa. Importance of molecular epidemiology is that it can offer clues as to how the virus spreads between the region and countries. Subtype C virus (of the M group) is prevalent in India. In Asia, HIV-1 isolates of subtypes E, C and B predominate.

About 5% of the infected persons progress to AIDS within 2 to 3 years and are called Rapid Progressors. About 5% of the infected persons do not progress to AIDS even after 10 years and are called Long Term Non Progressors. The reasons are being, mutant nef gene of HIV[6] and defective CCR-5 co-binding protein on the macrophage due to genetic abnormality in the patient.[7]

WHO Staging system for HIV infection

Clinical stage I	Clinical stage II	Clinical stage III	Clinical stage IV
1. Asymptomatic HIV infection 2. Persistent Generalized Lymphadeno-pathy 3.Primary HIV infection Performance-scale 1: Asymptomatic, Normal activity	1.Weight loss <10% of body weight 2. Minormuco-Cutaneous manifestations (seb.derm, fungalnail-infections, recurrent oral ulcers , angular chelitis) 3.Herpes zoster with in the past 5 years 4.Recurrent Upper Respiratory Infections (Bacterial sinusitis) And / or Performance-scale 2: symptomatic, Normal activity	1.Weight loss>10 % of body weight 2.Un explained Chronic diarrhoea > 1 month 3.Un explained prolonged fever (intermittent or constant) > 1 month 4.Oral Candidiasis 5.Oral hairy leckoplakia 6.Pulmonary tuberculosis 7. Severe Bacterial infections (pneumonia, pyomyositis) 8. Cervical intra epithelial neoplasia And / or performance - scale 3 : Bed-ridden, < 50 % of the day during past month	Candidiasis of the bronchi, trachea or lungs, Oesophageal candidiasis, Cervical cancer, Coccidioidomycosis, Cryptococcosis – (extra pulmonary), Cryptospori diosis – chronic intestinal (> 1 month duration), Isosporiasis – chronic intestinal (> 1 month duration), Cytomegalovirus disease (other than lung, spleen and nodes), CMV retinitis (with loss of vision), HIV encephalopathy, Herpes simplex- (chronic ulcer, bronchitis, pneumonia or Oesophagitis), Histoplasmosis – (disseminated or extra pulmonary), Kaposi's sarcoma, Lymphoma, MAC, M. kansasi infection – (pulmonary), disseminated, M.tuberculosis –extra pulmonary , disseminated Pneumocystis carinii pneumonia,

			Recurrent pneumonia, Progressive multi focal leuko encephalopathy, Salmonella septicemia – recurrent, Toxoplasmosis, Wasting syndrome And / or Performance - scale 4 : Bed-ridden > 50 % of the day during past month

Hepato – biliary abnormalities

In advanced HIV infected patients, with CD4 < 200 , Hepato – biliary abnormalities were noted, even though they are asymptomatic. In literature, it was stated that, such abnormalities were due to the CMV, Cryptospora , etc and no specific drugs were available and hence the role of ART was mentioned in such conditions[8]. Hence the present study was under taken, also to find out the response to ART, since ART centre was launched recently in our set-up.

In HIV infected patients, Liver diseases can be classified into four Groups :

1. Those that are associated with HIV related immune compromise and are rarely encountered in non immuno suppressed individuals [eg. AIDS cholangiopathy , Mycobacterium avium intracellurare (MAC) and Cyto Megalo virus (CMV) hepatitis]

2. Those that occur in both immuno compromised and immuno-competent individuals, but that are more prevalent in those who are HIV positive than those who are HIV negative [eg. HBV and HCV infection]
3. Drug- induced hepatotoxicity, which results from the multiple HIV specific ARV drugs and other antimicrobials.
4. All the common hepato-biliary diseases that afflict those who are HIV negatives [eg . gallstones – associated cholecystitis and alcoholic liver disease]

The advent of Anti retroviral therapy (ART/ARV) has revolutionized the management of HIV infection. From an incurable disease, highly active anti retroviral therapy has made HIV infection a treatable and chronically manageable illness.

In 1987, Zidovudine was reported to be useful in managing the patients with HIV infection for the first time.[9] The failure of monotherapy led to a focus on combination treatment with two nucleoside analogues.

The failure of long lasting clinical benefits with dual nucleoside analogue therapy and the development of protease inhibitors led to triple therapy with one protease inhibitor and two nucleoside analogues.

HAART combination consist of one protease inhibitor with two NRTIs or one NNRTI with two NRTIs.

In our ART centre, two NNRTIs (Nevirapine&Efavirenz), and three NRTIs (Zidovudine, Stavudine & Lamivudine) are available. We are using ART regimen including one NNRTI with two NRTIs.

WHO Recommendations for ART in adults with HIV infection

1. WHO stage IV irrespective of CD4 (Cluster of Differentiation) cell count.
2. WHO stage III with CD4 cell count <350 cells/ mm3.
3. WHO stage I & II with CD4 cell count <200 cells/ mm3.

Side effects of ARV Drugs

The use of highly active antiretroviral therapy (HAART) against HIV has become the standard of care. Hepatotoxicity has been noted with all of the protease inhibitors as well as many of the nucleoside and nonnucleoside analog drugs. A recent study compared the incidence of hepatotoxicity in patients receiving several different regimens with and without protease inhibitors and found that ritonavir was associated with a higher incidence of hepatotoxicity when compared with indinavir, nelfinavir, saquinavir, and nucleoside analog regimens.

Hepatic steatosis is another pattern of injury noted as a complication of HIV medications. Hepatic steatosis in the setting of

lactic acidosis has been described for zidovudine, didanosine, and now stavudine.

Nucleouside Reverse Transcriptase Inhibitors (NRTIs) are commonly associated with Hepatic steatosis. Non Nucleouside Reverse-Transcriptase Inhibitors (NNRTIs) usually cause Hepatitis. Protease - Inhibitors (PIS) are associated with Liver toxicity in the form of jaundice (hyperbilirubinemia and elevated liver enzymes)

AIMS & OBJECTIVES

1. To find out the hepato- biliary abnormalities in HIV positive patients.

2. To correlate hepato- biliary abnormalities with their CD4 counts.

3. To find out Hepatitis B and Hepatitis C co-infection in HIV patients.

4. To find out the response of the hepato- biliary abnormalities to Anti Retro Viral Therapy.

5. To detect Anti Retro Viral Therapy induced hepato- biliary abnormalities

REVIEW OF LITERATURE

Classification of Hepato-biliary abnormalities in HIV infection[10] :

1. Hepatic disorders are caused by

a) **Viral hepatitis**

Hepatits B (HBV)

Hepatits C (HCV)

b) **Opportunistic infections : (OI)**

1. Mycobacterium avium intracellulare (MAC)
2. Mycobacterium tuberculosis (Myc. TB)
3. Cytomegalo virus (CMV) (associated with biliary tract disease)
4. Herpes simplex virus
5. Ebstein Barr Virus (EBV)
6. Cryptococcus Neoformans (associated with biliary tract disease)
7. Histoplasmosis
8. Candida albicans (associated with biliary tract disease)
9. Cocidomycosis
10. Microspordia (associated with biliary tract disease)
11. Toxoplasmosis
12. Bacillary peliosis

c) **Tumors**

Hodgkin's & Non Hodgkin's Lymphoma

Kaposi's sarcoma

d) **Hepato toxic drugs :**

sulphonamides

ARV drugs : Nevirapine, Zidovudine etc

Antibiotics

INH

Anti fungals

Tranquillizers

Biliary disorders

AIDS Cholangiopathy

Lymphoma

Kaposi's sarcoma

Acalculus cholecystitis

Hepatic Disease in HIV based on CD4 Lymphocyte count[11]

CD4 Lymphocyte count	Predominantly Cholestatic	Predominantly Hepatocellular
500 or less	Drug toxicity Mycobacterium tuberculosis Kaposi's sarcoma Lymphoma Cholelithiasis Acalculus cholecystitis Bacterial abscess	Drug toxicity Steatosis Viral Hepatitis Herpes simplex
250 or less	Fungal infection Candidiasis Histoplasmosis Cryptococcosis Blastomycosis Cryptosporidium AIDS Cholangiopathy Bartonella/bacillary angiomatosis and peliosis	Pneumocystis carinii
100 or less	Cytomegalovirus Mycobacterium avium intracellulare Microspordia	Cytomegalovirus

Hepatitis B Virus infection :

Risk factors for acquisition of HBV infection are similar to those for acquisition of HIV infection. Both viruses have an increased

prevalence in persons with multiple sexual partners and in injection drug users.[12] Markers of prior or active HBV infection are present in more than 80% of patients with HIV infection, approximately 10% of whom are HBsAg positive, as described by Hollander et al.[13]. After acute infection with HBV, patients with HIV infection are at greater risk of developing chronic HBV infection than are those without HIV infection.

Compared with patients with HBV infection alone, HBV/HIV coinfected patients have higher levels of viral replication, lower serum ALT values, and milder histologic disease. Historically, HBV infection has not adversely affected survival in HIV-positive patients,[13] although with improving survival of HIV-infected patients, liver disease is emerging as an important clinical problem.

Coinfected patients have reduced rates of response to alpha-interferon. Data suggest that there is limited benefit of interferon alone in the setting of HIV. However, there are good response rate to lamivudine in co infected patients. Therefore, patients with evidence of actively replicating virus and liver disease should be considered for treatment.

Lamivudine administered at 100 mg/day is sufficient to control HBV, but HIV patients are often on higher doses given that lamivudine is also used as treatment for HIV at a dose of 300 mg/ day[14]. Unfortunately, mutation of HBV virus and subsequent resistance to lamivudine is

common. Currently, there are no additional drugs approved for the treatment of lamivudine resistant HBV. In HIV positive patients without serologic evidence of past or present HBV infection, vaccination is largely ineffective.

Hepatitis C Virus infection :

Coinfection with HCV and HIV is common, because of shared transmission routes. Berenguer and wright et al., observed that rates of HCV seropositivity ranging from 4% to 100% in their study, depending on the transmission category, with higher rates among injection drug users and recipients of blood transfusions than among men who have sex with men and heterosexual contacts.[15]

The clinical course of HCV infection in HIV patients is often more aggressive. Multiple studies have demonstrated an increased rate of fibrosis and prevalence of cirrhosis. chronic hepatitis C is a growing cause of morbidity and mortality in patients who are HIV positive. Indeed, several studies have shown that HIV/HCV–co infected patients have more severe liver injury and a worse prognosis than do patients with HCV infection alone.[15]

The reasons why hepatic decompensation develops more rapidly in coinfected patients than in those with HCV infection alone are unknown. Several hypotheses have been raised:

1) HIV does not seem to be cytopathic to hepatocytes, but it can be demonstrated in Kupffer cells in patients with AIDS and could have pathologic effects on the liver by stimulating abnormal production of fibrogenic cytokines;[16]

2) hepatic decompensation could be precipitated by AIDS-related opportunistic infections in patients who have already developed cirrhosis as a result of chronic HCV infection;

3) HIV immunosuppression enhances serum HCV RNA levels, which have been shown in some studies to be associated with more severe liver damage; and

4) Distribution of HCV genotypes and HCV diversity may be different in coinfected patients compared with those infected with HCV alone.

Additional specific features of HCV infection have been proposed to occur more frequently in coinfected patients as compared with patients infected with HCV alone. These include 1) lack of sensitivity of serologic assays in diagnosing HCV infection, 2) enhancement of HCV replication, and 3) higher risk of heterosexual and perinatal transmission of HCV infection. Data to support some of these observations are stronger than others. Interferon therapy may be tried, but will have the greatest benefit , only in those with higher CD4 counts with the modern therapy of HIV,

the number of doubly infected persons with good immune function will increase and combined ribavarin / interferon therapy can be tried[17].

Mycobacterium avium intracellulare :

Typically, this is a late-stage infection, and the liver involvement is part of systemic infection. The pathologic hallmark is the presence of poorly formed granulomas associated with large numbers of acid-fast bacilli within foamy histiocytes[18]. Acid-fast smear of infected tissue usually reveals organisms, although distinction from Mycobacterium tuberculosis is not possible by smear alone. Patients typically have systemic systems, including fever, lymphadenopathy, diarrhea, and night sweats. Associated bone marrow infiltration is common.

The diagnosis can often be established by blood culture, bone-marrow, or lymphnode examination prior to consideration of liver biopsy.[19] Imaging studies may reveal diffuse intra abdominal adenopathy. Liver abnormalities typically include disproportionate elevation of serum alkaline phosphatase,with modest elevation of bilirubin, AST and ALT, less frequently, hepatomegaly. The mean survival is only 69 days.

Mycobacterium tuberculosis :

Mycobacterium tuberculosis can occur at an earlier stage, and is more prevalent in injection drug users than in other categories. Granulomas are found in Liver biopsy specimen in about 25% of persons with pulmonary TB and 80% of those with extrapulmonary TB. Multiple

granulomas may also be seen in persons with impaired immune response. Reynolds et al., described about granulomatous hepatitis in AIDS patients[20] When the CD4>200, infection is pulmonary, where as atypical presentations, including hepatic involvement are seen in patients with severe immuno-deficiency.

Extra pulmonary tuberculosis, including liver disease, is more common in HIV infected patients, and may be manifested by abdominal pain, jaundice, or hepato splenomegaly[21]. Treatment of M.tuberculosis in HIV patients is same like others. But in our RNTCP program, we are giving either Category I or Category II[22]. Category III is not given for HIV patients. Rifamycins may induce CYP450; therefore, drug-drug interactions can be expected with HAART (PI and NNRTI)[23].

Cytomegalo virus infection:

Cytomegalo virus infection is late and part of generalized disease. It is associated with fever and weight loss. Diagnosis is made by demonstrating nuclear and cytoplasmic inclusions in Kupffer cells, bile duct epithelium and occasionally hepatocytes[24]. Mono nuclear cell-infiltration or neutrophils may be present.Non specific elevations of transaminases are noted. It also causes granulamatous hepatitis and Acalculous cholecystitis.

BACILLARY ANGIOMATOSIS

Bacillary Angiomatosis is an infectious disorder that primarily affects persons with AIDS or other immunodeficiency states. The causative agents have been identified as the gram-negative bacilli Bartonella henselae, which is difficult to cultivate and, in some cases, B.quintana.[25] Infection is frequently associated with exposure to cats.

Bacillary angiomatosis is characterized most commonly by multiple blood-red papular skin lesions, but disseminated infection with or without skin involvement has also been described.[26] The causative bacilli can infect liver, lymph nodes, pleura, bronchi, bones, brain, bone marrow, and spleen. Additional manifestations include persistent fever, bacteremia, and sepsis. Hepatic infection should be suspected when serum aminotransferase levels are elevated in the absence of other explanations.

Hepatic infection in persons with bacillary angiomatosis may present as peliosis hepatis, or blood-filled cysts. Histologically, peliosis in patients with AIDS is characterized by an inflammatory myxoid stroma containing clumps of bacilli surrounding the blood-filled peliotic cysts. Diagnosis of *Bartonella* infection by polymerase chain reaction–based methods is being used more often.[27] along with Warthin-Starry silver staining of infected tissue, chocolate agar culture

FUNGAL INFECTIONS:

Cryptococcal, coccidioidal, and histoplasmal infections are usually seen in association with systemic disease.[28,29] Liver involvement may be macro- or microscopic. Candida rarely infects the liver, despite its high prevalence in mucocutaneous sites. Hepatic Candida infections are confined to patients who are neutropenic, typically in response to systemic chemotherapy used to treat non-Hodgkin's lymphoma. Fungal infections especially histoplasma are associated with granulamatous hepatitis[30,31] Tashjian LS, Abramson JS, et al., studied about the occurrence of granumotous hepatitis in AIDS patients.[30]

PNEUMOCYSTIS CARINII INFECTION:

Rare cases of Pneumocystis carinii or microsporidial infection in the liver have been reported[32]. The presence of P carinii in extra-pulmonary sites typically is seen in patients who have had inhalation therapy with a drug such as pentamidine, which fails to protect sites outside the airways.

HIV INFECTION PER SE AND HEPATOBILIARY ABNORMALITIES

Typically, HIV is found within hepatic macrophages and occasionally sinusoidal endothelial cells. Infection of macrophages is not surprising, given the propensity of the virus to infect the cell type in other organs[16]. Nonetheless, infection of hepatic macrophages by HIV suggests

that the liver may be a large reservoir of virus. Additionally, HIV infection of Kupffer's cells could result in impaired cell function, leading to the increased incidence of enteric bacteremias in, this population. Despite the demonstration of HIV in liver, there is no discrete clinical syndrome of liver disease that has been ascribed to HIV alone.

Liver abnormalities commonly associated with drugs used in the treatment of HIV and its complications.

Predominantly Hepatocellular Disease	**Predominantly Cholestatic Disease**
Clarithromycin Delaviridine Didanosine (ddl) Efavirenz Dideoxycytidine (ddc) Indinavir Isoniazid Ketoconazole Nelfinavir Nevirapine Pentamidine Ritonavir Saquinavir Stavudine (d4T) Trimethoprimsulfamethoxazole Zidovudine	Rifampin Ketoconazole Trimethoprim- Sulfamethoxazole Dapsone

Drug Reactions Caused by drugs used in the management of HIV:

Drug Reactions are the commonest cause of Jaundice in AIDS[33] - Potentially hepatotoxic drugs frequently used in the management of HIV-positive patients are summarized in the previous Table. Liver abnormalities associated with most of these drugs are typically indicative of hepatocellular injury, although certain drugs are associated with a predominantly "cholestatic pattern of liver injury. The use of highly

active antiretroviral therapy (HAART) against HIV has become the standard of care.

Hepatotoxicity has been noted with all of the protease inhibitors as well as many of the nucleoside and nonnucleoside analog drugs. A recent study compared the incidence of hepatotoxicity in patients receiving several different regimens with and without protease inhibitors and found that ritonavir was associated with a higher incidence of hepatotoxicity when compared with indinavir, nelfinavir, saquinavir, and nucleoside analog regimens[34].

Fortgang et al., described hepatomegaly and steatosis with enzyme elevation in AIDS patients receiving Antiretroviral therapy and he further stated that more than 10 fold elevation of liverenzymes with symptoms of liverdysfunction are the indications to stop ART.[34] Hepatic steatosis is another pattern of injury noted as a complication of HIV medications.[34] Hepatic steatosis in the setting of lactic acidosis has been described for zidovudine, didanosine, and now stavudine. Lactic acidosis can be diagnosed clinically with the following features, abdominal pain, distension, vomiting, fatiguiability, weight loss. Lactic acid level is <2IU normally. More than 5IU is an indication to stop treatment.

Some patients have developed progressive, fatal hepatic steatosis. Typically, the syndrome has occurred in patients who appear to be

relatively well and has been ascribed to mitochondrial injury.[35] Two other frequently noted problems are sulfa allergy with associated liver toxicity and hyperbilirubinemia in the setting of indinavir. This is primarily an elevation in unconjugated bilirubin and is not related to liver injury.[36]

Immune Reconstitution syndrome

It is a paradoxical reaction characterized by Overt manifestation of sub clinical infection after 3-6 months of ART. It is due to improvement in CD4 levels after ART and is a good sign of recovery. Any opportunistic infections may manifest, the common ones being tuberculosis, herpeszoster etc., ART should not be stopped and should be continued along with the treatment of the underlying infections.

NEOPLASMS:

Non-Hodgkin's lymphoma:

Non-Hodgkin's lymphoma (now referred to as either large cell lymphoma or Burkitt's lymphoma, depending on the histologic findings) typically presents in extranodal sites, and occurs at all stages of HIV infection with equal frequency. The liver is among the more common extranodal sites; there may be focal hepatic lesions associated with pain, weight loss, night sweats, and a progressive rise in both alkaline phosphatase and transaminase levels.[37]

The lesion is typically identified by noninvasive imaging, and diagnosis can be established by an experienced pathologist using fine-needle aspiration and cytologic or conventional liver biopsy. The prognosis of non-Hodgkin's lymphoma is largely correlated with the stage of HIV infection and extent of immuno compromise. Although not strictly an AIDS- defining diagnosis, advanced-stage Hodgkin's lymphoma, often with visceral involvement, is also seen with increased prevalence in all risk groups.

Kaposi's sarcoma:

Kaposi's sarcoma is a neoplasm that is largely confined to skin and mucous membrances but can involve the liver. Recent evidence has revealed that greater than 85% of tumors are associated with a virus that has been named Kaposi's sarcoma-associated herpes virus (KSHV) or human herpesvirus 8 (HHV-8). Hepatic lesions are usually asymptomatic; however, there have been reports of bleeding from lesions following liver biopsy. Chemotheraphy or Radiotheraphy are the treatment options.

Biliary tract diseases :

AIDS Cholangiopathy :

It is a biliary syndrome diagnosed by clinical features, dramatic elevation of alkaline phosphatase, evidence of cryptospora in stools,

characteristic findings in ultrasonogram (USG), Computed Tomogram (CT) scan and Endoscopic Retrograde cholangio pancreatography (ERCP).[38] It is diagnosed by John cello in 1989. Amitsharma and Lalit Dugal et al., found out that estimated incidence of AIDS cholangiopathy was 45% in their study (including Asymptomatic).[38] It is common when CD4 count is <100.

HIV per se won't cause AIDS Cholangiopathy. Opportunistic infections contribute for 50-81% of the cases. Cryptospora, CMV, Microspora are the common organisms, others include Cyclospora, Isospora, MAC, salmonella, enterobacter, candida etc.[39] Pathogenesis is not clear, may be due to cytopathic effect over biliary epithelium, periductal inflammation and cholangiocyte apoptosis. AIDS Cholangiopathy is identified as following four entities.[40]

1. Papillary stenosis with common bile duct dilatation (>8 mm)
2. Sclerosing cholangitis (focal stricture and dilatation of intrahepatic with or without extrahepatic ducts)
3. Papillary stenosis and Sclerosing cholangitis
4. Long extrahepatic stricture (1-2cms long)

Clinical features of AIDS Cholangiopathy include fever, right upper quadrant pain, asymptomatic also. Jaundice is extremely unusual.[41] Marked elevation of alkaline phosphatase and normal or mild elevation of

ALP and AST are observed. ALP is a good prognostic indicator.[42] It is noted that Ultrasound has - 97% sensitivity & 100% specificity. Findings include common bile duct dilatation (>8 mm), terminal stenosis (distal Common Bile Duct (CBD) tapering 2-4mms), dilatation of intrahepatic & extrahepatic ducts and focal strictures, distention and wall thickening in gallbladder.

CT scan has highest diagnostic yield for dilatation. ERCP is gold standard. Cryptospora in stools, IgM Ab for CMV are the other useful tests. Anti Microbial Therapy has no effect over biliary tract.[39] Anti Retro viral Therapy is the treatment of choice. Surgical intervention like Sphincterotomy, stenting, cholecystectomy can be done in the presence of pain and obstruction.

Acalculous cholecystitis :

It is commonly caused by cytomegalovirus in HIV patients.[43] Patients present with severe abdominal pain with or without peritonitis. Wind P, Chevallier JM, et al., observed that cytomegalovirus is a common cause of Acalculous Cholecystitis.[44] It is surgical emergency. Cholecystectomy is the treatment of choice.

Non-Hodgkin's lymphoma, Kaposi's Sarcoma:

Rare cases of Non-Hodgkin's lymphoma or Kaposi's sarcoma have been reported in the biliary tree, reflecting the aggressive nature and unusual presentations of these neoplasms in this setting.

Materials and Methods

Setting	:	This study was carried out at Government Rajaji Hospital, Madurai
Collaborating Departments	:	Department of Medicine, Dept of Sexually Transmitted Diseases, ART Center, Dept of Medical Gastro Enterology
Study Design	:	Prospective study
Period of study	:	January 2005 - September 2006

Sample size and selection of study subjects :

The study was conducted in HIV positive patients, who were attending the ART Center, GRH, Madurai.

Among the patients attending ART Center, 100 patients who satisfied the inclusion criteria were included in the study and further evaluated.

Inclusion criteria:

1. Adult male and Non-pregnant female who are HIV positives.
2. Patients who are eligible for Anti Retro Viral Therapy Based on CD4 counts and WHO clinical staging.

Exclusion criteria:

1. Children
2. Pregnancy
3. Patients on Hepatotoxic drugs (Anti TB, Anti Epilepsy drugs, alcohol etc.,

Ethical issues :

The study group thus identified by the above criteria (Inclusion & Exclusion) were first briefed about the nature of the study .Willing participants were taken up, after getting a written informed consent from them.

Materials :

100 cases, who satisfied the inclusion & exclusion criteria above were taken up for the study.

Conflict of interest :

There was no conflict of interest.

Financial Support

No

Methodology

Selected Socio demographic, clinical and laboratory Data were elicited from the patients and recorded in a proforma.

1. Socio Demographic Data :

Economic and Educational Status and Demography

Age

Sex

2. Clinical Data :

clinical examination

3. Laboratory Data :

TC

DC

Hb%

ESR

Urine Albumin

Sugar

Deposits

CD4 count

Blood sugar

Urea

Serum creatinine

Serum electrolytes

LFT : Serum bilirubin – Total

Conjugated

Unconjugated

Serum Glutamate Oxalo Acetate Transaminase (SGOT)

Serum Glutamate Pyruvate Transaminase (SGPT)

Alkaline Phosphatase (ALP)

Serum proteins – Total

Albumin

Globulin

Hepatatis B Surface Antigen (HBsAg)

Anti HCV

UltraSonoGram - Abdomen

CT Scan - Abdomen (if required for further confirmation)

CD4 Count :

The standard method for enumerating CD4 T cells uses a flow cytometer. A computer calculates the number of CD4 T cells by analyzing the size of the cell and which of the antibodies , it has been tagged with. The over all process is called Fluorescence Activated Cell Sorting (FACS)

Statistical Analysis :

Data was entered in Microsoft excel spread sheet and analyzed. Statistically using standard statistical software.

AGE AND SEX DISTRIBUTION

Age	< 20	21- 30	31- 40	41- 50	>50
Males	2	5	44	9	4
Females	0	18	17	1	0

Of the 100 patients, 64 were males and 36 were females. The age ranged from 18 to 61 years in males with mean age of 35.58 years. Among the females, the age range was 24 to 43 years with average of 31.69 years.

Socio Demographic Data

Educational status

Level of education	Total No. of patients	Males	Females
Illiterate	36	18	18
Primary school	46	36	10
High school	14	8	6
Degree/ Diploma	4	2	2

Occupational Status

S. No	Occupation	Numbers
1	Cooly	34
2	Driver	11
3	Housewife	29
4	Clerk	4
5	Farmer	8
6	Others	14
	Total	**100**

Marital status:

Marital status	Male	Female	Total
Married	48	36	84
Unmarried	16	0	16

Investigations

S.no	Investigations	Range	Mean
1	Blood TC	4800 - 7400	6200
2	Blood Hb	7.6 – 10.8	9.2
3	Blood Sugar	60 - 312	89.6
4	Blood Urea	18 – 42	24.1
5	Serum Creatinine	0.7 – 1.4	0.93
6	CD4 Count	17 - 306	97.6
7	Pre ART Sr.Bilirubin	0.6 - 3	0.994
8	Pre ART Sr.Protien	4.6 – 6.4	5.796
9	Pre ART SGOT	17 - 134	32.5
10	Pre ART SGPT	11 - 142	33.72
11	Pre ART ALP	22 - 603	119.94
12	Post ART Sr.Bilirubin	0.6 – 1.1	0.816
13	Post ART SGOT	18 - 66	32.4
14	Post ART SGPT	17 - 117	39.14
15	Post ART ALP	35 - 284	98.08

Incidence of hepatobiliary abnormalities in AIDS.

Total incidence of hepatobiliary abnormalities is 15% in asymptomatic AIDS patients. Among this 15%, 2% had hepatic abnormalities, 8% had AIDS cholangioapathy. 4% had HBS Ag positivity and 1% had anti HCV positivity.

AGE, GENDER AND CD4 COUNT CORRELATION

	CD4 COUNTS							
	<50		**51- 100**		**101- 200**		**> 200**	
	Male	**Female**	**Male**	**Female**	**Male**	**Female**	**Male**	**Female**
<20	0	0	0	0	0	0	2	0
21 - 30	3	3	0	5	2	6	0	4
31 - 40	15	6	15	8	14	1	0	2
41 - 50	2	1	0	0	5	0	2	0
> 50	2	0	0	0	0	0	2	0
Total	22	10	15	13	21	7	6	6

Most of the patients (72%) were taking Zidovudine + Lamivudine + Nevirapine Regimen.

Others (28%) were on Stavudine + Lamivudine + Nevirapine Regimen.

CD_4 COUNT CORRELATION WITH HEPATOBILIARY ABNORMALITIES

CD_4 count	Hepatobiliary Abnormalities
<50	1% Anti HCV Positivity
50-100	6% AIDS Cholangiopathy 4% HBs Ag Positivity
100-150	2% AIDS Cholangiopathy 2% Hepatic Abnormalities
150-306	--

CD_4 count of the patients range from 17-306. All the patients having hepatobiliary abnormalities had CD4<150. 1% AntiHCV Positivity had CD_4<50. 6% AIDS Cholangiopathy and 4% HBs Ag Positivity had CD_4 between 50-100. 2% AIDS Cholangiopathy and 2% Hepatic Abnormalities had CD_4 between 100-150. So, CD_4 count has an inverse relationship with hepatobiliary abnormalities.

HIV – HBV co infection

	% of positivity	**Liver function tests**	**Ultra-Sonogram**	**CD4 Count**
HIV-HBV co infection	4%	2% with <2 fold increase in SGOT/SGPT	Normal	<100
HIV-HCV co infection	1%	Normal	Normal	<50

HBsAg Positivity was seen in 4 out of 100 HIV patients. Among these male : female ratio was 1:1 .All were asymptomatic . CD4 count was less than 100 in all 4 patients. Out of 4 patients, < 2 fold elevation of Pre ART SGPT was noted in 2 patients. But normal Post ART SGPT was seen in those 2 patients. Remaining 2 patients with normal Pre ART SGPT got <2fold elevation of Post ART SGPT. Sr. Bilirubin, Sr.Protein, ALP were normal in all 4 patients in Pre and Post ART. No Anti HCV positivity was noted in these 4 HbSAg positive patients. Ultrasonogram abdomen was normal in all these patients.

HIV-HCV co infection

Anti HCV positivity was noted in One male patient. He was asymptomatic . CD4 count was 46 cells. Pre ART LFT as well as Post ART LFT were within normal limits. HbSAg was negative. Ultrasonogram abdomen was also normal.

RESPONSE OF HEPATIC ABNORMALITIES TO ANTI RETROVIRAL THERAPY

Among 100 patients, 2 patients had > 2 fold elevation of SGOT / SGPT before starting ART and hepatomegaly in USG. Both of them had normal values after ART.

RESPONSE OF AIDS CHOLANGIOPATHY TO ANTIRETROVIRAL THERAPY

	SGOT			SGPT			ALP		
	M	**S.D.**	**'P' value**	**M**	**S.D**	**'P' value**	**M**	**S.D**	**'P' value**
Pre ART	39	12.26	0.011	48	22.06	0.035	342.5	182.97	0.035
Post ART	28.5	5.78		33.25	9.3		188.25	87.05	

M - Mean

S.D. - Standard Division

There is statistically significant difference between liver enzymes (SGOT/SGPT/ALP) in AIDS Cholangiopathy before and after ART. (According to WILCOXON SIGNED RANKS TEST, 'P' Value<0.05 is significant).

AIDS Cholangiopathy was noted in 8 % of cases. Male : Female ratio was 1:1 . 6 out of 8 patients had CD4 < 100. Remaining 2 had 100 – 120. All patients were clinically asymptomatic. LFT showed that marked elevation of ALP and normal SGOT & SGPT. Ultrasonogram showed Sclerosing Cholangitis, Papillary Stenosis and Thickening of CBD with Biliary Sludge. 2 cases had hepatomegaly also. HBsAg and Anti HCV were negative in all cases.

After HAART, ALP values come down, with the resolution of AIDS cholangiopathy.

ANTI RETROVIRAL THERAPY INDUCED SGOT / SGPT ELEVATION

In 6 patients, 2-3 fold elevation of SGOT / SGPT after ART was noted due to ART induced Liver enzyme elevation who had normal values before ART. 2 out of 6 patients had fatty liver in USG.

ALKALINE PHOSPHATASE ELEVATION AFTER ANTIRETROVIRAL THERAPY

2% of Patients had 2 fold ALP elevation, after starting ART, may be due to immune reconstitution or ART induced Liver enzyme elevation.

Ultra sound findings

30% had hepatomegaly and fatty liver. 15 out of 30 had elevation of liver enzymes also.

8% had AIDS cholangiopathy with Sclerosing cholangitis, papillary stenosis and thickening of CBD with Biliary sludge.

2% had gallstones with elevated billirubin

Incidently 2% were found have pancreatitis.

DISCUSSION

A study of Hepato – biliary abnormalities in 100 AIDS patients was done. In literature, it is stated that Hepatic disorders are due to Viral Hepatitis, Opportunistic infections, Tumors and Hepato toxic drugs[10]. In our study , 64 males & 36 females were included. Age ranged from 18 to 61 years, with most of them being illiterates and few had primary school level education. Most of them were married and house wives, majority were coolies by occupation.

Clinically all of them were asymptomatic. Their CD4 counts ranged from 17 to 306. Mean was 97.6. 72 % of patients were taking Zidovudine + Lamivudine + Nevirapine Regimen. Remaining 28 % were taking Stavudine + Lamivudine + Nevirapine Regimen. All were on cotrimoxazole for Opportunistic Infection (OI) prophylaxis.

Hepatobiliary abnormalities in AIDS Patients

Interpretation of Liver function tests :

Serum Billirubin was almost normal for all patients except very few who had gall stones. Serum albumin was normal for all. SGOT and SGPT were mildly elevated (< 2 fold) in many patients. Reynolds et al., described that hepatic abnormalities are commonly due to opportunistic infections like Myco TB, CMV, MAC etc and

upto 10% hepatic abnormalities were noted in their study.[20] In our study 2% of patients, who were asymptomatic had 2–3 fold elevation of SGOT/ SGPT with mild hepatomegaly (no echo pattern changes or focal lesions), before starting ART. Both of them had normal values after ART. This finding is suggested that they might have had opportunistic infections like CMV, MAC etc. which responded very well due to immune restoration after ART.

Amitsharma and Lalit Dugal et al., found out that estimated incidence of AIDS cholangiopathy was 45% in their study (including Asymptomatics).[38] In our study 8 % of patients had significant elevation (>4 fold) of ALP before starting ART, with ultrasound and CT confirming AIDS Cholangiopathy. All were asymptomatic. All of them had normal values after ART.

AIDS Cholangiopathy :

It is a biliary syndrome diagnosed by clinical, dramatic elevation of alkaline phosphatase, evidence of cryptospora in stools, characteristic findings in ultrasound, CT scan and ERCP. Estimated incidence is 45% including asymptomatics[38]. It is common when CD4 count is <100. HIV per se won't cause cholangiopathy.

Opportunistic infections contribute for 50-81% of AIDS Cholangiopathy. Cryptospora, CMV, Microspora are the common organisms. Others include Cyclospora, Isospora, MAC, salmonella,

enterobacter, candida etc. Jaundice is extremely unusual. Marked elevation of alkaline phosphatase and normal or mild elevation of ALP and AST are observed. ALP is a good prognostic indicator. In our study, 8 % of cases who were asymptomatic had elevation of ALP (> 4 folds) with characteristic Ultrasound findings suggestive of cholangiopathy. 6% of patients had CD4 < 100. Remaining 2% had 100 – 120. In literature it is stated that, Ultrasound has 97% sensitivity & 100% specificity. Findings include common bile duct dilatation (>8 mm), terminal stenosis (distal CBD tapering 2-4mms), dilatation of intrahepatic & extrahepatic ducts and focal strictures, distention and wall thickening in gallbladder[40].

CT scan has highest diagnostic yield for dilatation. ERCP is the gold standard. In our study, USG abdomen had 100 % sensitivity & 100% specificity. We noted Sclerosing Cholangitis, Papillary Stenosis and Thickening of CBD with Biliary Sludge. Anti Microbial Therapy has no effect over biliary tract. Anti Retro viral Therapy is the treatment of choice. Our patients responded very well to ART as evidenced by normalization of ALP and disappearance of the USG / CT findings within 3-5 months of ART.

Ultra Sonogram Abdomen :

30 % of cases had either fatty liver or hepatomegaly with out focal lesion. This is due to either ART drugs toxicity (hepatic steatosis) or opportunistic infection like MAC , CMV etc. Gramse et al. observed that

10-12% of AIDS Patients had USG evidence of Sclerosing Cholangitis , Papillary Stenosis in their study.[40] In our study 8% of cases had Sclerosing Cholangitis , Papillary Stenosis and Thickening of CBD with Biliary Sludge suggestive of AIDS Cholangiopathy. 2 % of cases had gall stones. Incidentally, 2% of cases were found to have features suggestive of pancreatitis.

CD4 Correlation with hepatobiliary abnormalities

CD4 has an inverse relationship with hepatobiliary abnormalities, since opportunistic infections are commonly observed whenever the CD4 count decreases.

Forbes et al., observed that AIDS Cholangiopathy is common when CD4 count is <100[41]. In this study 6% of AIDS Cholangiopathy had CD4 <100 and 2% of the same had CD4 100-120. 2% of hepatic abnormalities (Elevation of SGOT / SGPT elevation with hepatomecaly) had CD4 between 100-120. 4% of HBsAg positivity had CD4 <100 and 1% of HCV positivity had CD4 <50.

HBV and HCV Co-infection in HIV Patients

HIV – HBV Co infection:

In literature, it is stated that Both viruses have an increased prevalence in persons with multiple sexual partners and in injection drug users.[12] Markers of prior or active HBV infection are present in more than 80% of patients with HIV infection, approximately 10% of whom

are HBsAg positive, as described by Hollander et al.[13]. But in this study , we have noted , only 4 % were HBsAg positive with the possible mode of transmission being sexual route. Reason being injection drug users are less common in our set up. All were asymptomatic with no signs of liver cell failure. CD4 count was less than 100 in all 4 patients. Liver function tests including serum protein were within normal limits except mild elevation (< 2 fold) of SGPT.

Ultra Sonogram Abdomen was also normal. Anti HCV was negative. Co infected patients are at greater risk of developing chronic HBV infection like Chronic active hepatitis and Cirrhosis. Patients with evidence of actively replicating virus and liver disease should be considered for treatment. Lamivudine administered at 100 mg/day is sufficient to control HBV. In our study, we did not observe any active liver diseases. Our patients were on HAART due to AIDS. They were getting Lamivudine at a dose of 150 mg Twice daily.

HIV – HCV Co Infection:

Berenguer and wright et al., observed that rates of HCV seropositivity ranging from 4% to 100% in their study, depending on the transmission category, with higher rates among injection drug users and recipients of blood transfusions than among homosexual men and heterosexual contacts.[15] In our study, only 1% was noted, with the possible mode of transmission being sexual route. Injection drug users

are less common in our set up. All were asymptomatic with no signs of liver cell failure. CD4 count was 46 cells. Liver function tests were within normal limits. UltraSonogram Abdomen was also normal. HBsAg was negative. The clinical course of HCV infection in HIV patients is often more aggressive. Multiple studies have demonstrated an increased rate of fibrosis and prevalence of cirrhosis.

Chronic hepatitis C is a growing cause of morbidity and mortality in patients who are HIV positive. Indeed, several studies have shown that HIV/HCV–co infected patients have more severe liver injury and a worse prognosis than do patients with HCV infection alone.[15] Our patient didnot have active liver disease. But, he was on HAART due to AIDS.

Antroviral therapy induced hepatobiliary abnormalities

Fortgang et al., described hepatomegaly and steatosis with enzyme elevation in AIDS patients receiving Antiretroviral therapy and he further stated that more than 10 fold elevation of liver enzymes with symptoms of liver dysfunction are the indications to stop ART.[34] In this study, 8% of patients had Liver enzymes elevation–6% with SGOT/SGPT elevation and 2% with ALP elevation. Out of Total 8%, in 6 % of patients, 2-3fold elevation of SGOT / SGPT after ART was noted who had normal values before ART. They were taking Nevirapine, Lamivudine, Zidovudine or Stavudine, and co-trimoxazole for OI Prophylaxis. This is due to either drug toxicity or immune reconstitution. They are continuing drugs, but

they are under observation. Liver abnormalities associated with most of these drugs are typically indicative of hepatocellular injury, although certain drugs are associated with a predominantly cholestatic pattern of liver injury.

ALP was mildly elevated (<2 fold) in many patients. Out of Total 8% of ART induced enzyme elevation, in 2 % of patients, significant elevation of ALP (2-3 fold) after ART was noted who had normal values before ART. This is mainly due to immune reconstitution or drug toxicity.

LIMITATIONS

1. Liver biopsy was not attempted due to ethical reasons.

2. HIV viral load could not be estimated due to constraints.

3. Specific diagnostic tests for individual opportunistic organisms, such as Motion culture for cryptospora, CMV IgM ab testing, ERCP for cholangiopathy, were not done.

4. HBeAg, HBV DNA,HCV RNA were not done.

CONCLUSIONS

1. The incidence of definite hepatobiliary abnormalities in AIDS supported by both USG and biochemical findings was 15% in asymptomatic patients, but USG alone suggested 30% incidence of the same. Among the 15% of patients with hepato- biliary abnormalities, 2% had hepatic involvement (SGOT/SGPT elevation with hepatomagaly), 8% had biliary (AIDS-Cholangiopathy) 4% had HBs Ag Positivity and 1% with anti HCV positivity.

2. It was observed that CD4 count and hepatobiliary abnormalities had inverse relationship. Of 8% patients with HIV cholangiopathy, 6% had CD4 < 100 and 2% had CD4 100-120. 2% of patients with hepatic abnormalities (SGOT/SGPT elevation with hepatomegaly) had CD4 between 100-120. All the 4% pts with hepatitis B had CD4 < 100 and 1% hepatitis C had < 50.

3. The incidence of HIV – HBV coinfection was 4% and HIV–HCV coinfection was 1%, all patients were asymptomatic with no evidence of active liver disease.

4. 2% of hepatic abnormalities (SGOT/SGPT elevation with hepatomegaly) and 8% of AIDS cholangiopathy responded very well to 3 to 5 months of ART.

5. Incidence of significant POST ART hepatobiliary abnormalities was 8% with 6% having 2-3 fold SGOT, SGPT elevation and 2% having 2 fold ALP elevation, which warranted only a close follow up but not ART withdrawal.

SUMMARY

The present study was undertaken with an aim to find out hepato-biliary abnormalities in AIDS patients, with CD4 count correlation, HBV, HCV coinfection with HIV and the response of hepato-biliary abnormalities to ART including ART induced hepato-biliary abnormalities. 100 AIDS Patients after satisfying inclusion and exclusion criteria were included in the study and they were evaluated regarding hepato- biliary abnormalities.

In our study, 64 males & 36 females were included. Age ranged from 18 to 61 years, with most of them being illiterates and few had primary school level education. Most of them were married and house wives, majority were coolies by occupation. Clinically all of them were asymptomatic. Their CD4 counts ranged from 17 to 306. Mean was 97.6. 72 % of patients were taking Zidovudine + Lamivudine + Nevirapine Regimen. Remaining 28 % were taking Stavudine + Lamivudine + Nevirapine Regimen.

The incidence of definite hepatobiliary abnormalities in AIDS supported by both USG and biochemical findings was 15% in asymptomatic patients, but USG alone suggested 30% incidence of the same. Among the 15% of patients with hepato biliary abnormalities, 2% had hepatic involvement (SGOT/SGPT elevation with hepatomagaly),

8% had biliary(AIDS Cholangiopathy) 4% had HBs Ag Positivity and 1% with anti HCV positivity. It was observed that CD4 count and hepatobiliary abnormalities had inverse relationship. Of 8% patients with HIV cholangiopathy, 6% had CD_4 < 100 and 2% had CD_4 100-120. 2% of patients with hepatic abnormalities (SGOT/SGPT elevation with hepatomegaly) had CD_4 between 100-120. All the 4% pts with hepatitisB had CD_4 < 100 and 1% hepatitis C had < 50.

The incidence of HIV-HBV co-infection was 4% and HIV–HCV co-infection was 1%, with the possible mode of transmission being heterosexual route, all patients were asymptomatic with no evidence of active liver disease. 2% of hepatic abnormalities (SGOT/SGPT elevation with hepatomegaly) and 8% of AIDS cholangiopathy responded very well to 3 to 5 months of ART. Incidence of significant POST ART hepatobiliary abnormalities was 8% with 6% having 2-3 fold SGOT, SGPT elevation and 2% having 2 fold ALP elevation, which warranted only a close follow up but not ART withdrawal.

APPENDIX – 1

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APPENDIX - 2

PROFORMA

Name : Age : Sex : Wt :

Address : Education:
Occupation :

Complaints :

H/o Present illness :

H/o jaundice / high coloured urine / pale stools / itching / abdominal pain
H/o nausea / vomiting / fever
H/o haematemesis / malena / other bleeding manifestations
H/o distension of abdomen / swelling of legs / dyspnoea
H/o oral lesions / dysphagia / diarrhoea
H/o skin rashes

H/o Past illness :

H/o jaundice / blood transfusion
H/o diagnosis of HIV : when : where :
Reason for testing :
Mode of transmission :
H/o ART : Started on : Regimen :
Adherence :
H/o TB / ATT
H/o epilepsy / Anti convulsants
H/o any other chronic drug intake
H/o DM / HT

Personal History :

Smoker / Alcoholic : duration :
stopped / not
Drug abuse :

Family History :

H/o HIV positivity in spouse / children
H/o ART : spouse / children
H/o jaundice in family members

General Examination :

Built / Nourishment / Conciousness / Orientation
Anaemia /Jaundice / Cyanosis / Clubbing
Pedal edema / Generalized lymphadenopathy
Spider naevi / Palmar erythema
Gynaecomatia / Testicular atrophy
Temp : PR : BP : RR :
Oral cavity : OC / OHL / Aphthous ulcers
Gingivitis / Pharngitis / Herpes labialis
Hyper pigmentation of tongue / buccal mucosa
Skin : IBA / PPE / Seb.derm / Scabies
Fungal infection / Herpes zoster / Impetigo
CVS : S1,S2+ Murmur :
RS : NVBS + Added sounds :

Abdomen : soft / moves with respiration / tenderness
distended / not
dialated veins / not
free fluid / not

Organomegaly : **Liver :** **Spleen :**
Size :
Extension :
Margin :
Moves with respiration :
Surface :
Consistency :
Tenderness :
Bruie :
External genitalia : Any genital lesion / Inguinal nodes

Investigations :

Blood TC :	DC :	Hb :
Urine Alb :	Sug :	Dep :
Blood Sugar :	Urea :	S.Creatinine :
Blood VDRL :	ELISA :	
CD4 count :	CD8 :	Ratio :
	Pre ART	Post ART

LFT :

S. bilirubin - Total
Direct
Indirect
SGOT
SGPT
ALP
Serum Protein
HbSAg
HCV
USG Abdomen : Liver :
- Span
- Echo pattern
- Focal lesion
- IHBR dilatation
- Portal vein

GB :
- wall thickening
- focal lesion
- peri GB fluid
- calculus
- CBD

Pancreas :
- size & echo pattern
- focal lesion
- calcification
- pancreatic duct

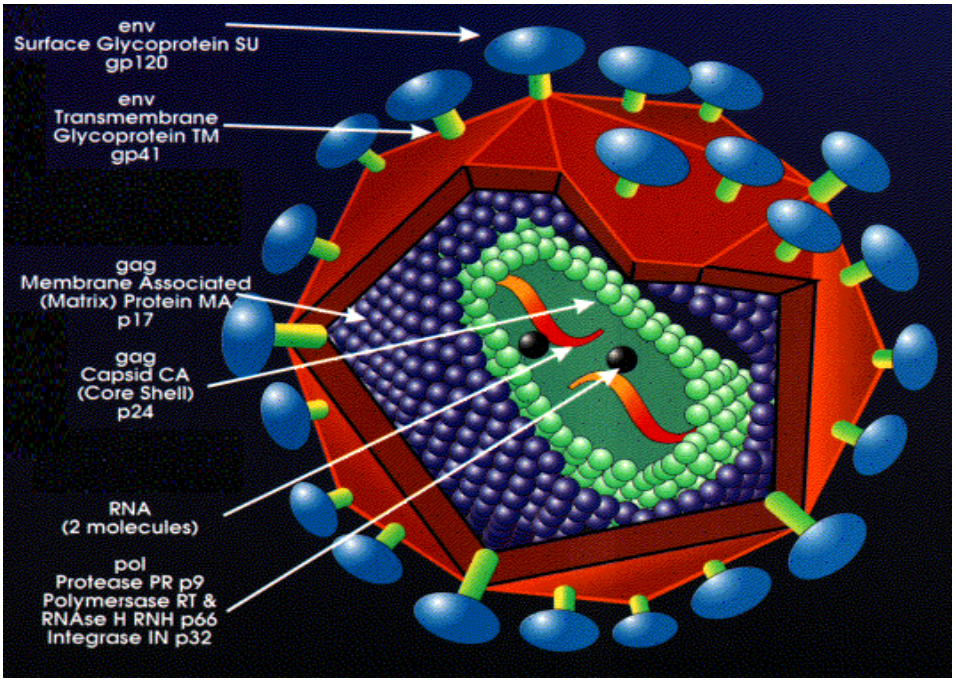
Spleen :
- size & echo pattern
- focal lesion

APPENDIX – 3

ABBREVIATIONS

AIDS	-	Acquired Immuno Deficiency Syndrome
ART / ARV	-	Anti retroviral therapy
ALP	-	Alkaline phosphatase
CBD	-	Common Bile Duct
CMV	-	Cyto megalo Virus
ERCP	-	Endoscopic Retrograde cholangio pancreatography
HAART	-	Highly active Anti retroviral therapy
HIV	-	Human Immuno Deficiency Virus
HCV	-	Hepatitis C Virus
HBV	-	Hepatitis B Virus
Myco TB	-	Myco Bacterium Tuberculosis
MAC	-	Myco Bacterium Avium Intracellulare
NRTI	-	Nucleoside reverse transcriptase inhibitors
NNRTIS	-	Non Nucleoside reverse transcriptase inhibitors
OI	-	Opportunistic infections
PIS	-	Protease inhibitors
STD	-	Sexually transmitted diseases
SGOT	-	Serum Glutamate Oxaloacetate Transaminase
SGPT	-	Serum Glutamate Pyruvate Transaminase

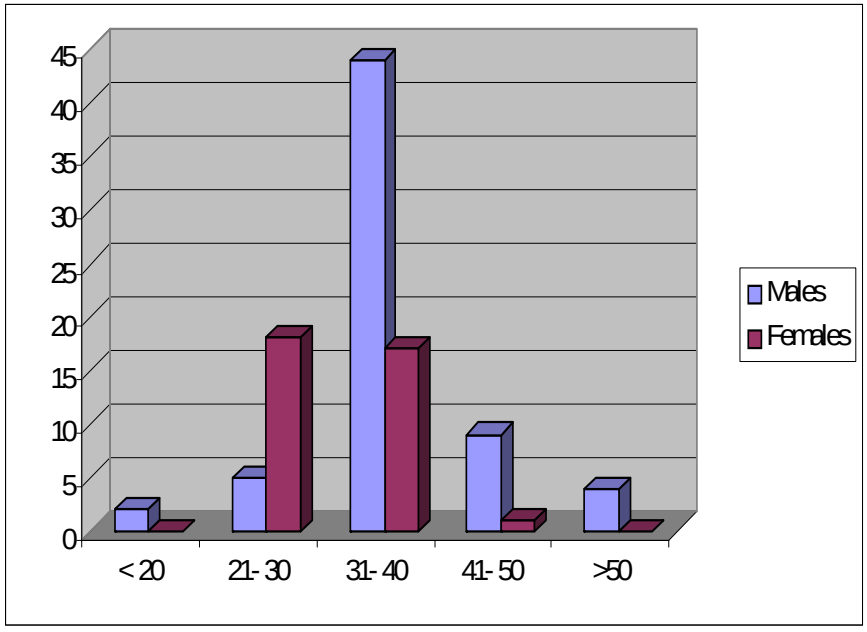
HIV Virus Structure

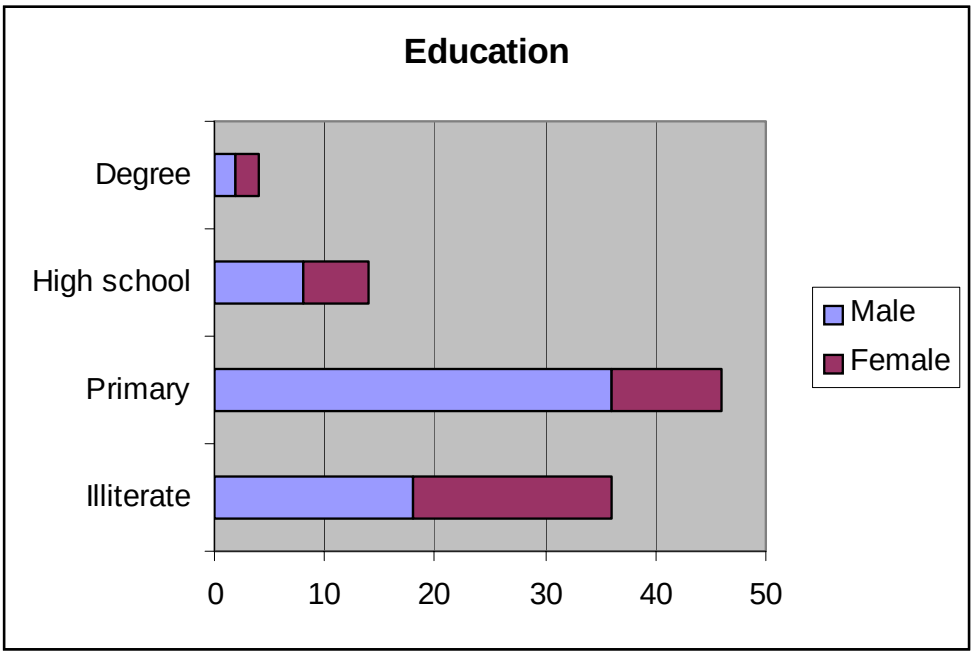


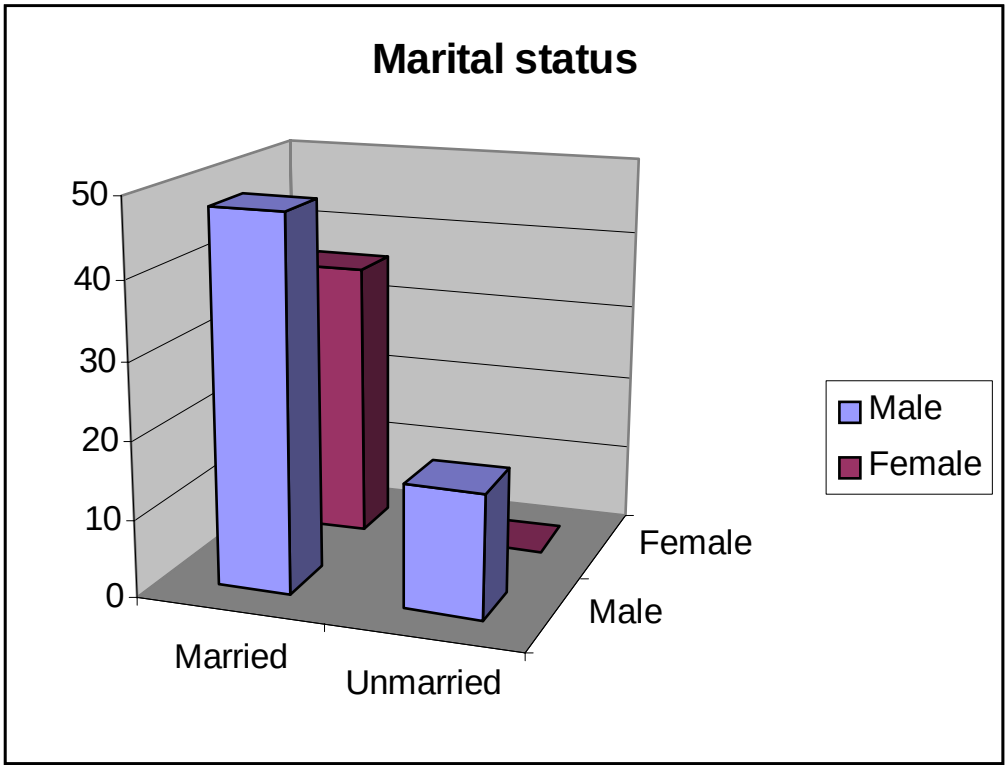
Virology & Lab Testing

Slide 4

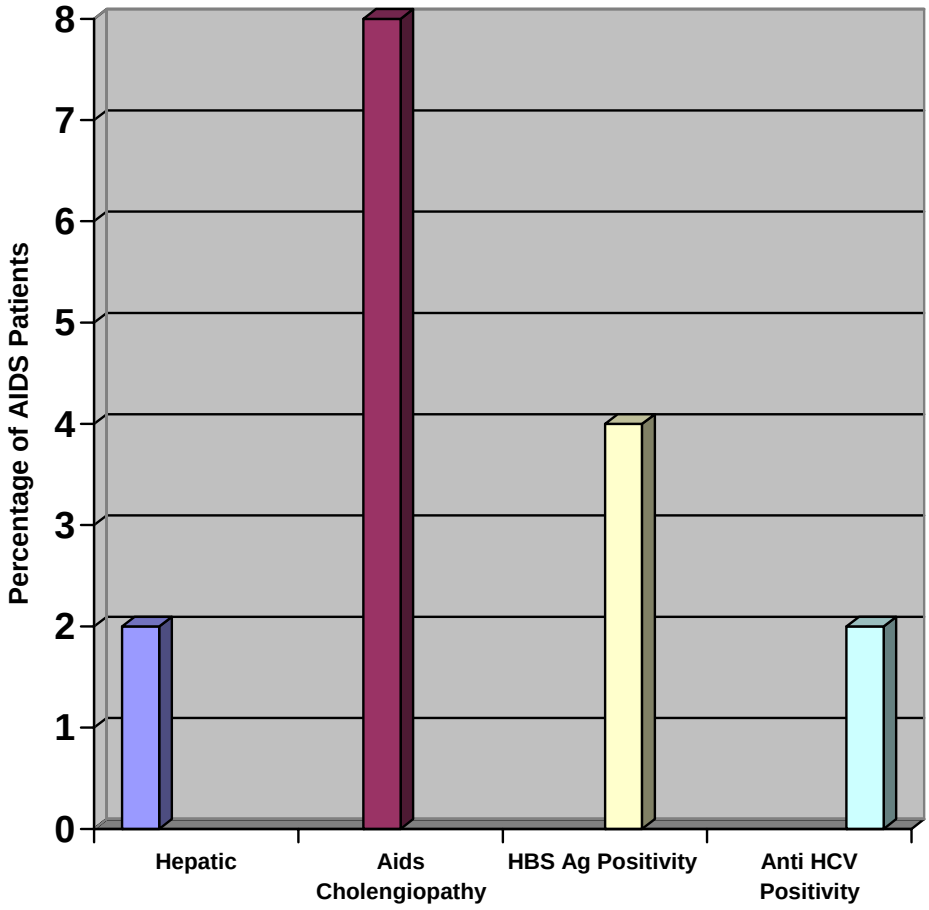
AGE AND SEX DISTRIBUTION




Education
Degree
High school
Primary
Illiterate
0
10
20
30
40
50
Male
Female

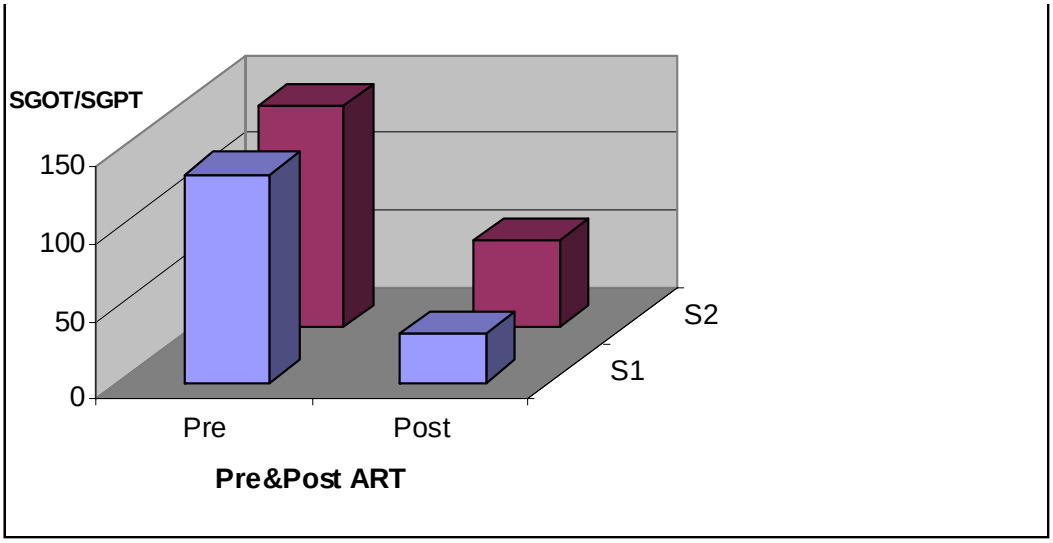

Marital status
50
40
30
20
10
0
Married
Unmarried
Female
Male
Male
Female

Incidence of hepatobiliary abnormalities in AIDS.

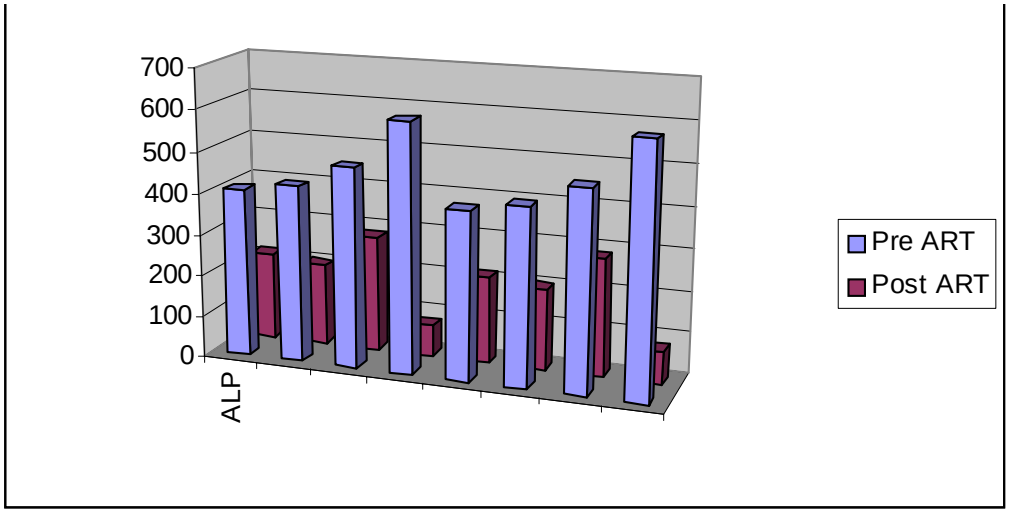


RESPONSE OF HEPATIC ABNORMALITIES TO

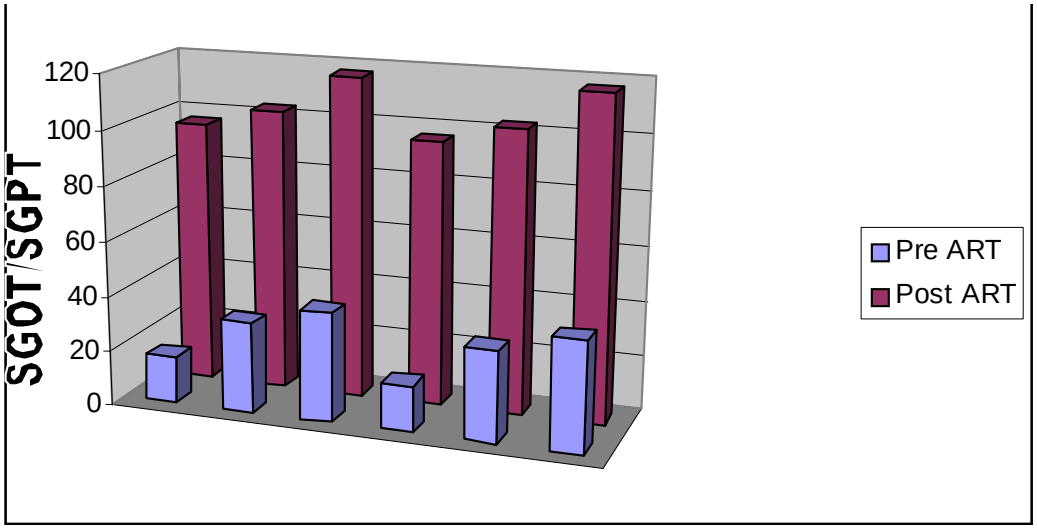
ANTI RETROVIRAL THERAPY



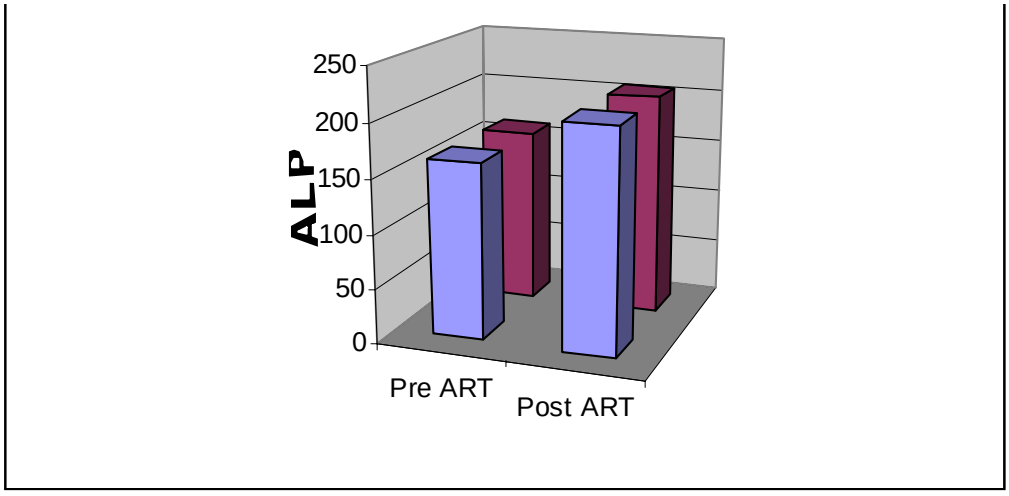
RESPONSE OF AIDS CHOLANGIOPATHY TO ANTI RETROVIRAL THERAPY

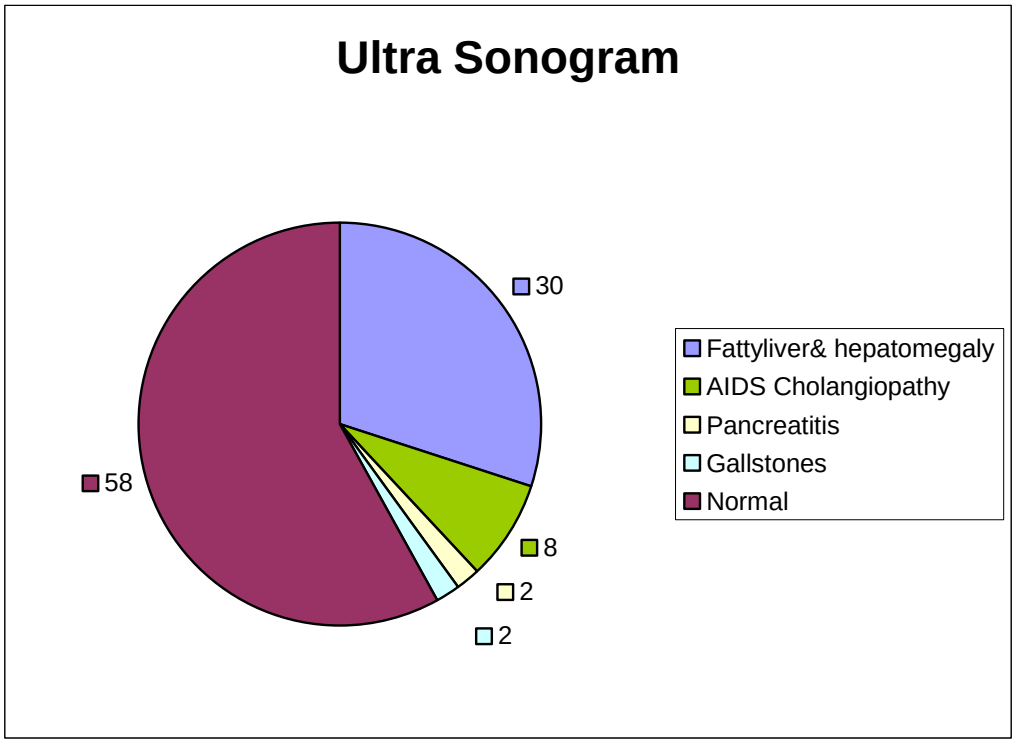


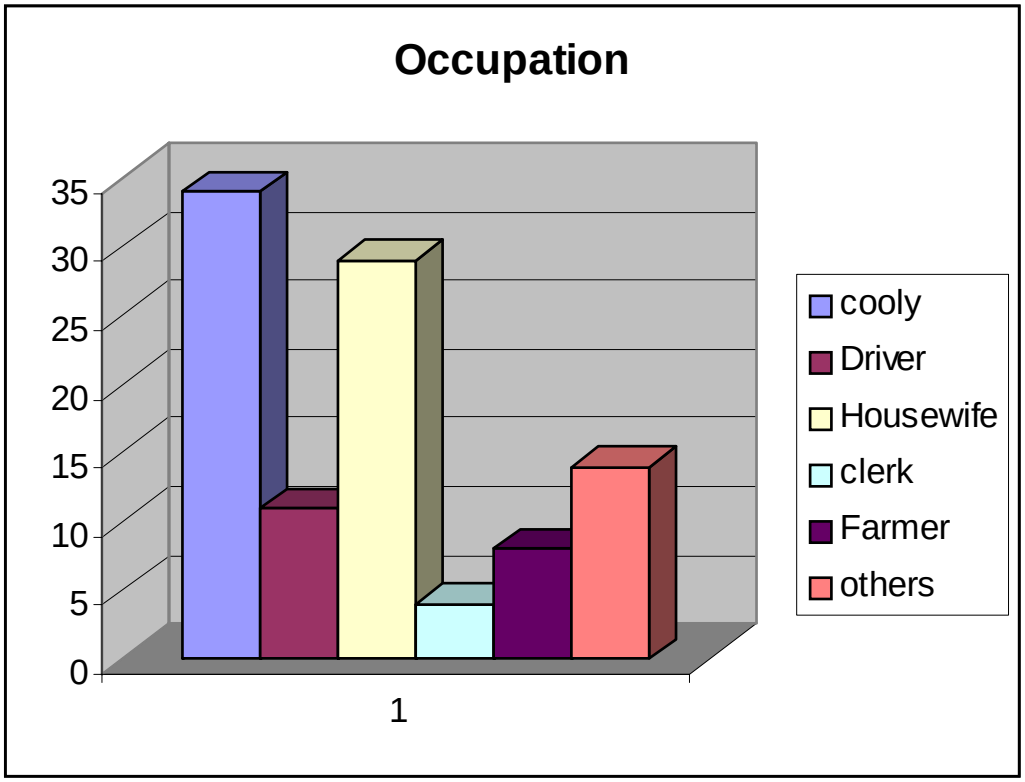
ANTI RETROVIRAL THERAPY INDUCED SGOT / SGPT ELEVATION



ALKALINE PHOSPHATASE ELEVATION AFTER ANTIRETROVIRAL THERAPY




Ultra Sonogram
30
8
2
2
58
Fattyliver& hepatomegaly
AIDS Cholangiopathy
Pancreatitis
Gallstones
Normal


Occupation
35
30
25
20
15
10
5
0
1
cooly
Driver
Housewife
clerk
Farmer
others